wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using polymerase chain reaction.

9. (Amended) A method according to [claim 7] any one of claims 26-32, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

11. (Amended) A method according to [claim 10] any one of claims 33-39, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using polymerase chain reaction.

12. (Amended) A method according to [claim 10] any one of claims 33-39, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks. Following the amendments, claims 8, 9, 11, 12 and 26-39 are pending in the application, with claims 26-39 being in independent format.

The specification has been amended to update the reference to related applications and to correct a minor typographical error. The pending claims have been amended in response to the Examiner's objections and to more clearly define certain aspects of the applicants' invention. Claims 7 and 10 have been cancelled from the application and rewritten as newly added claims 26-39. Newly added claims 26-32 are drawn to methods for detecting the presence of prostate cancer in a patient comprising contacting a biological sample obtained from the patient with an oligonucleotide that hybridizes to SEQ ID NO:45, 67, 107, 308, 311, 313 or 326, respectively, under moderately stringent conditions. Newly added claims 33-39 are drawn to

methods for monitoring the progression of a cancer in a patient comprising contacting a biological sample obtained from the patient with an oligonucleotide that hybridizes to SEQ ID NO:45, 67, 107, 308, 311, 313 or 326, respectively, under moderately stringent conditions. In the methods of claims 26, 27, 29, 32, 33, 34, 36 and 39, the biological sample is selected from the group consisting of blood, serum and semen. It is submitted that support for this aspect of the claims may be found on page 20, lines 2-5, and throughout the specification as originally filed. Claims 8 and 9 have been amended to depend upon newly added claims 26-32. Claims 11 and 12 have been amended to depend upon newly added claims 33-39. It is urged that support for all the above amendments may be found throughout the specification as originally filed and that none of the amendments constitute new matter.

Applicant notes that the pending claims have been granted the priority date of January 15, 1999, the filing date of the subject patent application. The polynucleotides of SEQ ID NO:45 and 67 were first disclosed in U.S. Application 08/904,809, filed August 1, 1997. The polynucleotide of SEQ ID NO:107 was first disclosed in U.S. Application No. 09/020,747 filed February 9, 1998. Applicants thus request that claims 26, 27, 33 and 34 be granted the priority date of August 1, 1997, and that claims 28 and 35 be granted the priority date of February 9, 1998.

The pending claims stand rejected under 35 USC §112, first paragraph, as lacking an adequate written description. Specifically, the Examiner has stated that the claims "are broadly drawn to a genus of nucleic acid molecules that encompass a larger nucleic acid."

Following the above amendments, the pending claims are drawn to methods for detecting the presence of prostate cancer, or monitoring the progression of a cancer, in a patient comprising contacting a biological sample obtained from the patient with an oligonucleotide primer or probe that hybridizes to the polynucleotides of SEQ ID NO:45, 67, 107, 308, 311, 313 or 326. It is urged that one of skill in the art, on being provided with the instant specification, would indeed believe that the applicants were in possession of the presently claimed invention at the time the application was filed, and that this rejection of the claims under 35 USC §112, first paragraph, may be properly withdrawn.

The pending claims stand rejected under 35 USC §112, second paragraph, as being indefinite. Specifically, the Examiner has objected to the terms "oligonucleotide that

hybridizes to a polynucleotide" and "polynucleotide that hybridizes to the oligonucleotide," and to claims 7 and 10 as reciting non-elected sequences.

As noted above, the pending claims have been amended to clarify that the recited oligonucleotides hybridize to the elected sequences, and that the recited polynucleotides hybridize to the oligonucleotides, under moderately stringent conditions. A definition of moderately stringent conditions is provided on page 7, lines 19-25 of the specification. The pending claims have been amended to remove reference to non-elected sequences.

It is urged that one of skill in the art, on being provided with the instant specification, would clearly be able to determine the metes and bounds of the amended claims, and that this rejection of the claims under 35 USC §112, second paragraph, may be properly withdrawn.

The pending claims stand rejected under 35 USC §101 as lacking a specific and substantial asserted utility, and under 35 USC §112, first paragraph, as lacking an enabling disclosure. This rejection is respectfully traversed.

In response to the Restriction Requirement, applicants elected the species of SEQ ID NO:45 (referred to as P20), 67 (referred to as P80, also known as P704P), 107 (referred to as F1-12, also known as P504S), 308 (referred to as P712P), 311 (referred to as P775P), 313 (referred to as P710P) and 326 (referred to as P703PDE5). SEQ ID NO:326 represents an extended cDNA sequence of the clone P20 (see page 50, line 29 – page 51, line 3, of the specification). The full-length sequence of P703PDE5 is referred to as P703P. As taught throughout the specification, each of these polynucleotides may be employed to diagnose prostate cancer by means of polymerase chain reaction and/or *in situ* hybridization techniques.

As disclosed in the specification, using microarray analysis F1-12 was found to be over-expressed in prostate tumor, with expression being low or undetectable in all other tissues tested (see page 47, lines 12-13); and P775P and P710P were over-expressed in prostate tumor but not in normal prostate (page 51, lines 11-22), with little or no expression being seen in all other normal tissues. As evidenced by the attached declaration of Dr. Ray Houghton, the over-expression of F1-12 and P710P in prostate tumor compared to all normal tissues tested was confirmed using real time PCR. It is thus urged that the polynucleotides of SEQ ID NO:107 (F1-

12), 311 (P775P) and 313 (P710P) may indeed be employed to detect the presence of prostate cancer in a biological sample.

As disclosed in the specification, using RT-PCR P20 was found to be over-expressed in normal prostate and prostate tumor tissue compared to all normal tissues examined, with a modest increase in expression being observed in breast tumor, colon tumor and lung tumor (see page 49, lines 11-14); and P80 was found to be over-expressed in prostate tumor and normal prostate compared to all other normal tissues tested (see page 49, lines 26-28). The specificity of P20 and P703P expression is further evidenced by attached declaration of Dr. Ray Houghton. Using microarray analysis, P712P was found to be over-expressed in prostate tumor and many normal prostate tissue samples, with expression being low or undetectable in all other normal tissues (see page 51, lines 11-22, of the specification).

It is well known to those of skill in the art that prostate cells are not found in the blood of normal healthy individuals. However, when an individual is afflicted with prostate cancer, the prostate tumor is able to break through the membrane surrounding the prostate thereby permitting both normal prostate and prostate tumor cells to enter the capillaries and get into the blood stream. Thus the presence of either normal prostate or prostate tumor cells in the blood or serum of an individual is indicative of the presence of prostate cancer. Similarly, the presence of either normal prostate or prostate tumor cells in the blood or serum after removal of the prostate in a patient previously diagnosed with prostate cancer is indicative of the presence of residual disease. It is thus not necessary for an antigen to be prostate-tumor specific in order for it to be effective in diagnosing prostate cancer, rather it is sufficient for the antigen to be prostate-specific. The effectiveness of prostate-specific antigens in the diagnosis of prostate cancer is evidenced by the current wide-spread use of Prostate Specific Antigen (PSA), to diagnose and monitor the presence of prostate cancer. It is thus urged that polynucleotides comprising SEQ ID NO:45 (P20), 67 (P80), 308 (P712P) and 326 (P703PDE5) may be usefully employed to detect the presence of prostate cancer in a blood, serum or semen sample.

Furthermore, it is urged that it would be well within the capabilities of someone of skill in the art, on being provided with the instant specification, to practice the claimed methods. Applicants submit that the pending claims fully satisfy both the utility requirements of 35 USC

§101 and the enablement requirements of 35 USC §112, first paragraph, and that the rejections of the claims may be properly withdrawn.

The pending claims stand rejected under 35 USC §102(a) as being anticipated by WO 98/37418 and WO 98/37093. Specifically, the Examiner states that these two references teach the claimed methods utilizing polynucleotides of SEQ ID NO:45, 67 and 107. This rejection is respectfully traversed.

Both the WO 98/37418 and WO 98/37093 references were published on August 27, 1998. As noted above, SEQ ID NO:45 and 67 should be properly granted a priority date of August 1, 1997, and SEQ ID NO:107 should properly be granted a priority date of February 9, 1998. Both of the publications cited by the Examiner were published after these priority dates, and therefore do not constitute prior art to SEQ ID NO:45, 67 and 107. Applicants respectfully submit that the rejection of the claims under 35 USC §102(a) may thus be properly withdrawn.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

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JEP:sds
Enclosures:
Postcard
Check
Form PTO/SB/17 (+ copy)
Petition for an Extension of Time (+ 2 copies)
Declaration of Raymond L. Houghton, Ph.D.

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